



Modulating rheological and degradation properties of temperature-responsive gelling systems composed of blends of PCLA–PEG–PCLA triblock copolymers and their fully hexanoyl-capped derivatives[☆]

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ABSTRACT

In this study, the ability to modulate rheological and degradation properties of temperature-responsive gelling systems composed of aqueous blends of poly(ϵ -caprolactone-co-lactide)-*b*-poly(ethylene glycol)-*b*-poly(ϵ -caprolactone-co-lactide) (PCLA-PEG-PCLA) triblock copolymers (i.e. uncapped) and their fully capped derivatives was investigated. Uncapped and capped PCLA-PEG-PCLA triblock copolymers, abbreviated as degree of modification 0 and 2 (DM0 and DM2, respectively), were composed of identical PCLA and PEG blocks but different end groups: namely hydroxyl and hexanoyl end groups. DM0 was synthesized by ring opening polymerization of *l*-lactide and ϵ -caprolactone in toluene using PEG as initiator and tin(II) 2-ethylhexanoate as the catalyst. A portion of DM0 was subsequently reacted with an excess of hexanoyl chloride in solution to yield DM2. The cloud point and phase behaviour of DM0 and DM2 in buffer as well as that of their blends were determined by light scattering in a diluted state and by vial tilting and rheological measurements in a concentrated state. Degradation/dissolution properties of temperature-responsive gelling systems were studied *in vitro* at pH 7.4 and 37 °C. The cloud points of DM0/DM2 blends were ratio-dependent and could be tailored from 15 to 40 °C for blends containing 15 to 100 wt.% DM0. Vial tilting and rheological experiments showed that, with solid contents between 20 and 30 wt.%, DM0/DM2 blends (15/85 to 25/75 w/w) had a sol-to-gel transition temperature at 10–20 °C, whereas blends with less than 15 wt.% DM0 formed gels below 4 °C and the ones with more than 25 wt.% DM0 did not show a sol-to-gel transition up to 50 °C. Complete degradation of temperature-responsive gelling systems took ~100 days, independent of the DM0 fraction and the initial solid content. Analysis of residual gels in time by GPC and ¹H-NMR showed no chemical polymer degradation, but indicated gel degradation by dissolution. Preferential dissolution of lactoyl-rich polymers induced enrichment of the residual gels in caproyl-rich polymers. To the best of our knowledge, degradation of temperature-responsive gelling systems by dissolution has not been reported or hypothesized as being the consequence of acylation of polymers. In conclusion, blending of PCLA-PEG-PCLA triblock polymers composed of identical backbones but different end groups provides for a straightforward preparation of temperature-responsive gelling systems with well-characterized rheological properties and potential in drug delivery. Furthermore, acylation of triblock copolymers may allow for the design of bioerodible systems with control over degradation by polymer dissolution.

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1. Introduction

Hydrogels composed of copolymers containing polyester and poly(ethylene glycol) (PEG) are of general interest for biomedical

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and pharmaceutical applications as they are biocompatible and biodegradable, while also possessing properties such as injectability, crystallinity and network mesh size, which are easy to modulate [1–6]. Triblock copolymers made up of PEG as the middle block flanked by two aliphatic polyester blocks form, in aqueous medium, flower-like micelles in the low concentration range [7]. At higher concentrations and above critical gel temperature, polymers rearrange to form viscoelastic hydrogels [8,9]. Such temperature-responsive gelling systems are developed as injectable drug